Remarks

Claims 2, 4-5, 19, 20 have been cancelled.

Claims 3, 6, 11, 13, 17, 22-23, 25 and 28-32 remain in the application.

Claims 3, 13, 17, 25, 28, and 29 have been amended.

35 USC 103

The rejection of claims 25, 28, 31 and 32 as being unpatentable over Della Valle et al. in view of Merck and Schroten has been traversed by amending independent claims 25 and 28 to include further limitations.

Claims 25 and 28 now include the limitations previously found in claims 19 and 29, that GD3 be present as the predominant ganglioside from among the total gangliosides present in the mixture, and thus the minimum percentage of 50% by weight GD3 is specified. Aside from finding support in claims 19 and 28, the description also supports this limitation in paragraph [00245], where 50% GD3 is recited, as well as in the examples in which a mixture of gangliosides is used in which GD3 is present as the predominant ganglioside. In paragraph [00253], an example of 80% GD3 is stated, consistent with the "at least 50%" limitation.

This restriction is not taught or implied in the publication of Della Valle et al. (U.S. Patent No. 5,190,925 or "the '925 patent") because no formulation described by Della Valle et al. exceeds 50% GD3 as a fraction of total gangliosides. In the specific formulation described in column 8 (line 19) of the '925 patent, GD3 is a very minor component representing only 2% of total ganglioside. Further, in Table 1 found in column 5 of the '925 patent (lines 42-50), GD3 is not mentioned as one of the four main brain gangliosides with which the '925 patent is most concerned. In the table bridging columns 7 and 8, the typical formulation percentages provided permits GD3 in the range of from 1.0 to 2.5 % by weight. There is no implication that Della Valle et al. envisioned a formulation that could go beyond this and comprise at least 50% GD3.

The Examiner's assertion that Chagas' disease is an "inflammatory disease" is not accurate, and even if it could be considered to broadly fall within this category, the independent claims 25 and 28 clearly state that the mediating of inflammation is specifically for treating (1) inflammatory bowel disorders, (2) disorders arising from allergic responses, (3) diseases involving epithelial surface responses, or (4) inflammation of the intestine, retina, or neuronal tissue". These specific categories do not encompass Chagas' disease, which is a tropical parasitic disease known to be caused by the parasite Trypanosoma cruzi. Ultimately, the condition may result in congestive heart failure. Inflammation that may result from Chagas' disease could not possibly be attributed to any of the 4 categories of conditions outlined in independent claims 25 and 28. Chagas' disease is not an inflammatory bowel disorder, nor does it arise from an allergic response. Chagas' disease is not one known to involve epithelial surface responses, and nor is it known for an inflammatory effect on the intestine, retinal or neuronal tissue. The claims are clearly directed to mediating inflammation

for treating one of these four specific categories of conditions, and thus treatment of Chagas' disease is not encompassed by the independent claims.

The Examiner is reminded that while "mediating inflammation" is recited in the preamble, a further limitation on what is meant by "mediating inflammation" can be found in each independent claim. This limitation excludes treatment of Chagas' disease as one of the possible ways in which inflammation may be mediated.

Regardless of whether Chagas' disease can be transmitted transplacentally, as may be described in Merck, this teaching would not provide the limitations missing from the teachings of Della Valle et al. to permit a skilled person to arrive at the subject of claim 25 or 28, or any claim depending therefrom.

The reference of Schroten teaches the use of a ganglioside-containing formulation as protection against and prevention of allergies. The Applicants point out that with the last response, the term "prevention" was removed from the claims, and thus the currently claimed subject matter of the instant application should be considered mutually exclusive of the teachings of Schroten. Although Schroten teaches a formulation that may be protective against development of allergies, there is no insinuation that a ganglioside formulation could in any way mediate inflammation that would arise as a result of an allergic response. Prevention and protection per se occur prior to an allergy becoming apparent and prior to onset of any allergic response. Thus, prevention is clearly distinguishable from treatment of a condition (such as inflammation) that may result once an allergic reaction has occurred. There is no example within Schroten that involves treatment of an allergic condition or a symptom of an allergic reaction. The Applicants believe that this prior art document relating to prevention has no relevance to claims of the instant application directed to mediating inflammation.

The Examiner has provided, with the Office Action of November 5, 2008, a great deal of jurisprudence to establish that prevention and treatment of disease should be considered distinct undertakings and that a method of treating does not reasonably provide enablement for prevention. The Applicants assert that the converse is also true: that a document teaching only a method of prevention does not teach or reasonably suggest that the same method would result in an effective treatment.

The objection to claims 2-7, 11, 13, 17, 19-23, 25 and 28-32 as unpatentable in view of Ettinger when taken in combination with Pan et al., and the Merck Manual of Diagnosis and Therapy is believed to be traversed by the amendments made to each of the independent claims (claims 13, 25 and 28). As emphasized above, each claim now stipulates that GD3 be present at the level of at least 50%. With the limitations in place in the instant claims on the meaning of mediating inflammation as: comprising changing lipid components in microdomains for "treating inflammatory bowel disorders, disorders arising from allergic responses, diseases involving epithelial surface responses, or inflammation of the intestine, retina, or neuronal tissue", it is emphasized that Ettinger has neither provided a formulation in which GD3 is the predominant ganglioside, nor provided a ganglioside formulation to address any of the four stated categories of conditions from which the inflammation arises.

While Ettinger teaches a reduction in the number of gastrointestinal disease producing organisms using a ganglioside formulation, there is no implication that mediating inflammation per se is treatable. Turning to the formulation itself, there is no implication that a fraction containing GD3 is considered for use in this document. GM1, GD1a and GT1 fractions are all

considered, but there is no implication that GD3 may be a possible candidate for use in a formulation, much less the predominant ganglioside in the formulation, as now stipulated in each independent claim of the instant application. The Examiner has conceded on page 5 of the action that specific gangliosides and amounts are not described by Ettinger. However, the use for which the ganglioside formulation is intended also differs between the instant application and Ettinger. The study of Pan et al. that simply describes ganglioside composition from various sources does not make any implication of the use to which ganglioside formulations may be directed. Thus, the combination of Ettinger and Pan et al. together would not permit a skilled person to arrive at the subject matter of the claims. By merely combining teachings of Merck regarding E. coli infection as a cause for inflammation with Pan et al. and Ettinger, there is no further incentive for a person skilled in the art to arrive at the claimed invention.

35 USC 102

To overcome the objection that certain claims are anticipated by either Williams et al., Berger et al., or Schroten, independent claim 25 now includes limitations not described in these references. The limitations included in claim 25 are described above, and thus are not re-iterated here. Similarly, due to the limiting amendments made to claim 25, those claims depending from claim 25, specifically claims 17 and 23 (claim 19 now being combined with claim 25) would also be free of the applied anticipation rejection. In particular, an adult dose limit for gangliosides is now recited in claim 25, together with the stipulation that GD3 is present in an amount of at least 50% of the total gangliosides.

Lowering cholesterol per se is not the object of any of the applied references. The Applicants disagree with the Examiner's assertion that the delivery of the composition of Williams et al. to a subject would have inherently lowered the cholesterol level, and thereby renders claims 17, 23 and 25 anticipated. By amendment claim 25 to include the limitation of previous claim 19 (to which this particular objection had been raised), this objection is nevertheless traversed.

Williams et al. describes buffalo milk gangliosides and a procedure for their isolation. The document reports that GD3 is present in the buffalo milk ganglioside component, but does not report its presence in amounts of over 50% of total ganglioside as now stipulated in the claims of the instant application. Nor is there any suggested dose level as now found in the instant claim set. The disclosure of Williams et al. makes no attempt to quantify GD3. The emphasis is placed on GM1 in the description, and no particular mention of the benefit of GD3 presence in at least 50% of the composition is implied. In particular, Example 4 attributes the benefit of gangliosides from buffalo milk to binding of cholera toxin to binding with GM1. In paragraph number [0182] it is stated:

> [0182] In summary, the GM1 isolated from buffalo milk exhibits the functionality of bovine brain GM1. It may be inferred that GM1 from buffalo milk is as efficient in preventing toxin binding to small intestine cells as other GS species of the GM1 class. The GM1 from buffalo milk may prevent symptoms and infection of the small intestine originating from Vibrio cholerae"

This indicates that no skilled person would arrive at the invention as now claimed in claim 25 on the basis of this reference.

Turning to the reference of Berger et al., this document outlines a ganglioside containing composition that is colostrum-derived and which shows binding activity toward pathogens. This is not the subject of claim 25, or the claims depending therefrom, and thus because claim 25 relates to cholesterol lowering, it should be considered distinguishable from Berger et al. Further, there is no suggestion by Berger et al. that the gangliosides provided in the colostrum of the hyperimmune milk product should be predominantly GD3 (as recited in claim 25). The mention of GD3 is made only in the context of it being one of two gangliosides (GM3 and GD3) found in the product, but not in the context of it being the predominant ganglioside. These differences should traverse the objection raised.

Regarding the Schroten reference, rationale put forward above applies, and is not fully reiterated here. Simply because a ganglioside composition is proposed as a preventative strategy against allergies does not illustrate efficacy in mediating inflammation that may arise from an allergic reaction.

35 USC 103 (for dependent claims relating to claims 25)

To overcome the objection that certain claims are rendered obvious by the teachings of Williams et al., and/or Berger et al., independent claim 25 now includes limitations not described in these references. The limitations included in claim 25 are described above, and thus are not re-iterated here. Due to the limiting amendments made to claim 25, those claims depending from claim 25, to which the obviousness objection was raised would now also be free of the obviousness rejection.

Double Patenting

The Examiner rejected Claim 25 and the claims that depend there from on the ground of nonstatutory obviousness-type double patenting as being unpatentable over (1) claims 1-5 of U.S. 6,998,392 and (2) claims 9-17 of co-pending Application No. 11/622858.

In view of the amendments to Claim 25, applicants kindly request reconsideration and withdrawal of the double patenting and provisional double patenting rejections because the present claims contain limitations not found in claims 1-5 of U.S. Patent No. 6,998,392 or in the co-pending Application No. 11/622858.

A Request for Continuing Examination and fee accompany this Response.

Respectfully submitted,

DUANE MORRIS LLP

Robert M. Gould, Ph.D.
Reg. No. 43,642
Customer No. 76223
312-499-6706

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